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Research Article

Postoperative Thyroid Function Status in Children Undergoing Cardiac Surgery for Congenital Heart Disease

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Abstract

Background and Objective: The thyroid hormones influence on all metabolic pathways. After heart surgery using cardiopulmonary bypass (CPB), serum levels of thyroid hormones (T3 and T4) and thyroid stimulating hormone (TSH) are reported to decline which adversely affects metabolic pathways. This study was aimed to assess the postoperative thyroid function status in children undergoing cardiac surgery for congenital heart disease.

Materials and Methods: This quasi-experimental study (without control) was conducted in Dhaka Shishu Hospital (DSH), Dhaka over a period of 24 months between January 2012 to December 2013. A total of 20 children with congenital heart diseases who underwent cardiac surgeries were consecutively included. To assess the levels of thyroid hormones, such as triiodothyronine (T3), thyroxin (T4) and TSH, blood samples were collected from all patients on admission and at 24 and 72 hours postoperatively. The observation at 72 hours after operation was the end-point of this study.

Result: The mean age of the children was 3.5 (2.5 - 4.5) years. A male preponderance was observed in the series. Over two-thirds (70%) of the children had cyanotic congenital heart disease. Half of the children had ventricular septal defect (VSD) followed by Tetralogy of Fallot (30%) and Atrial Septtal Defect (ASD) (20%). The mean cardiopulmonary bypass (CPB) and aortic cross-clamp time were observed to be 84.9 and 50.8 minutes respectively. The ionotropic drugs dopamine, dobutamine, milrinine and adrenaline were generally used preoperatively. The mean ICU stay was 3.1 ± 0.7 days and the mean left ventricular ejection fraction (LVEF) was 59.5%. The serumT3 level at baseline (before operation) was 1.32 pico-mol/L which decreased to < 0.6 pmol/L after 24 hours of operation and again slightly increased to 0.75 pmol/L after 72 hours of operation. The T4 level at baseline about 88 pmol/L which reduced to 61.1 pmol/L after 24 hours and further reduced to 55.0 pmol/L after 72 hours of operation. Likewise serum TSH was decreased from 4.5 pmol/L at baseline to 2.9 pmol/L at 24 hours and 2.3 pmol/L at end-point.

Conclusion: The present study concluded that the changes in the thyroid hormones, that is, decrease in T3, T4 and TSH are influenced by cardiac surgery using CPB. It is recommended that thyroid hormones be measured before and after operation in patients with congenital heart disease for better postoperative management.

Keywords: *Congenital Heart Disease; Cardiac Surgery; Thyroid Hormones; Cardiopulmonary Bypass*

Introduction

Thyroid hormone has a wide range of cardiovascular effects which are mediated at both genomic and non-genomic levels. As a stress response to surgery, the non-thyroidal illness (NTI) syndrome or euthyroid sick syndrome occurs in the post-operative period following

cardiac surgery [1]. The cardiovascular impacts of the thyroid hormones may include increased contractility and cardiac output and reduced vascular resistance, all of which occur through several mechanisms [2-4].

The mechanism of transient hypothyroidism following CPB is influenced by hemodilution, endogenous factors such as glucocorticoids, tumor necrosis factor, and interlukin-6, or exogenous factors like dopamine administration [1]. In the postoperative period, with the deterioration of the patient's condition, the hypothalamic-pituitary-thyroid axis is suppressed, which in turn, leads to a reduction in serum free T4 [5]. In addition, because of the inhibition of type-1 monodeiodinase activity in non-thyroidal tissues, the production of T3 from T4 is hampered. As a result of this reduction, the thyroid function is compromised during postoperative period which in severe cases may induce mortality [6].

Low cardiac output syndrome and heart failure due to postoperative hypothyroidism occur at the same time as T3 is suppressed, especially within the first 48 postoperative hours [7,8]. The administration of T3 at this stage is quite likely to improve heart failure and increase cardiac output [9].

Aim of the Study

The present study is aimed to investigate whether children with congenital heart disease undergoing cardiac surgery using CPB compromise of thyroid functions postoperatively.

Materials and Methods

This quasi-experimental study (without control) was conducted in Dhaka Shishu Hospital (DSH), Dhaka over a period of 24 months between January 2012 to December 2013. Having obtained ethical clearance from the Ethical Review Committee of the abovementioned hospital, 20 children with congenital heart diseases who were scheduled to undergo cardiac surgeries (total correction of Tetralogy of Fallot, ventricular septal defect and atrial septal defect closure) using CPB were consecutively included. The exclusion criteria comprised the disease of other organs (e.g. liver, kidney, and central nervous system), endocrine abnormalities prior to hospitalization, and the use of any drugs that could influence the status of the thyroid hormones such as glucocorticoids, phenytoin, growth hormones, gonadal steroids, propylthiouracil, and Levothyroxine. The diagnosis (VSD, ASD, TOF etc.) and type (cyanotic or acyanotic) of congenital heart disease were confirmed before being scheduled for operation.

To assess the levels of thyroid hormones, such as triiodothyronine (T3), thyroxin (T4) and TSH, blood samples were collected from all patients on admission and at 24 and 72 hours postoperatively. The observation at 72 hours after operation was the end-point of this study. The serum was separated from the blood by centrifugation and stored at 2 - 7ºC until assay. The serum concentration of the hormones was measured via the Enzyme-Linked Immunosorbent Assay (ELISA) using (Monobind Company kits). Other pertinent information, such as, demographic characteristics (e.g. age and gender) and cardiac surgery-related information (e.g. CPB time, aortic cross-clamp time), postoperative hemodynamic status in the intensive care unit (ICU), duration of ICU stay (days), and the postoperative use of inotropic drugs were obtained from the patients' files.

Collected data were analyzed using SPSS (Statistical Package for Social Sciences) 17 for Windows (SPSS Inc., Chicago, Illinois). The categorical data were expressed as frequency (number) with corresponding percentage (%) and continuous data were expressed as mean ± SD. Repeated measure analysis of variance (ANOVA) was employed to analyze whether changes in thyroid hormonal made over time (from baseline to end-point of the study) were significant. The level of significance was set at 0.05 p-value < 0.05 was considered as statistically significant.

Results

The mean age of the children undergoing cardiac surgery for congenital heart disease was 3.5 (2.5 - 4.5) years. Males were predominant in the series with male to female ratio being 7:3. Over two-thirds (70%) of the children had cyanotic congenital heart disease. In terms of diagnosis, ventricular septal defect (VSD) ranked first (50%) followed by Tetralogy of Fallot (30%) and Atrial Septal Defect (ASD) (20%) (Table 1). Table 2 shows the distribution of pertinent preoperative variables. The mean cardiopulmonary bypass (CPB) and aortic cross-clamp time were observed to be 84.9 and 50.8 minutes respectively. Dopamine, dobutamine and milrinine were invariably used during operative period, while adrenaline was used in 80% cases (Table 2).

Demographic and baseline characteristics	Frequency	Percentage	Mean ± SD (range)
Age			3.5 ± 0.7 (2.5 - 4.5 years)
Sex			
Male	14	70.0	
Female	6	30.0	
Type of CHD			
Cyanotic	6	30.0	
Acyanotic	14	70.0	
Diagnosis			
ASD	4	20.0	
VSD	10	50.0	
TOF	6	30.0	

Table 1: *Comparison of demographic and baseline characteristics between groups.*

Preoperative variables	Frequency	Percentage	Mean ± SD (range)
Cardiopulmonary bypass (CPB) time (min)			84.9 ± 1 3.4 (56 - 110)
Aortic cross clamp (AOX) time (min)			50.8 ± 10.9 (36 - 75)
Dopamine	20	100.0	
Dobutamine	20	100.0	
Adrenalin	16	80.0	
Milrinine	20	100.0	

Table 2: *Distribution of preoperative variables.*

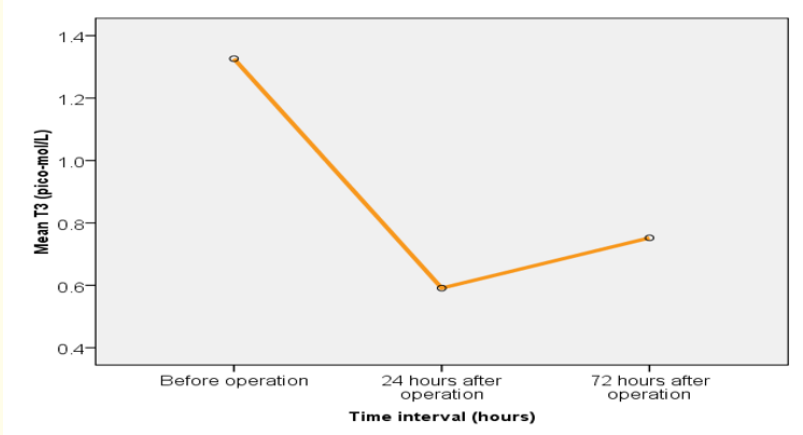
The mean ICU stay was 3.1 ± 0.7 days and the left ventricular ejection fraction (LVEF) was 5.9 2.5% (Table 3). The serum T3 level at baseline was 1.32 pmol/L which decreased to < 0.6 pmol/L after 24 hours of operation and again slightly increased to 0.75 pmol/L after 72 hours of operation. The T4 level at baseline was about 88 pmol/L which reduced to 61.1 pmol/L after 24 hours and further reduced to 55.0 pmol/L after 72 hours of operation. Likewise serum TSH was decreased from 4.5 pmol/L at baseline to 2.9 pmol/L at 24 hours and 2.3 pmol/L at 72 hours of operation (Table 4).

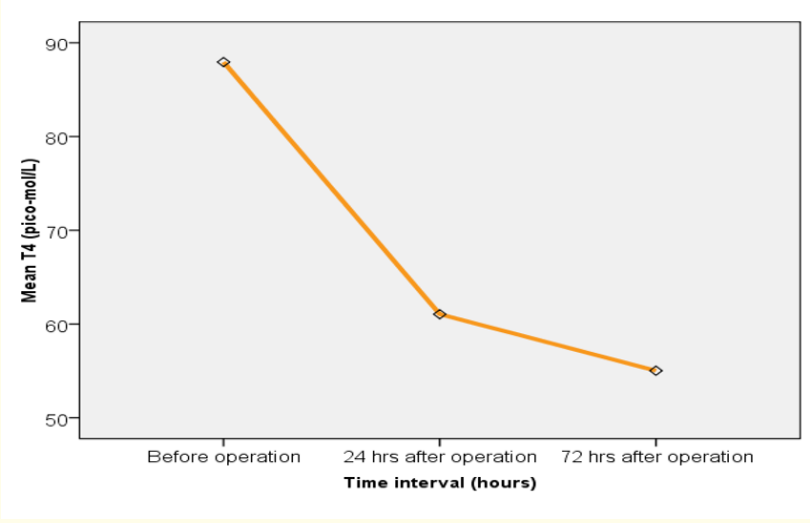
Outcome	Mean	SD	Range
ICU stay (days)	3.1	0.7	2 - 4
LVEF (%)	59.0	2.5	53 - 62

Table 3: *Outcome of the children undergoing cardiac surgery.*

Serum thyroid hormones	Time interval (hours)			p-value
	Before operation	24 hrs after operation	72 hrs after operation	
T3 (pmol/L)	1.32 ± 09	0.59 ± 0.05	0.75 ± 0.52	< 0.001
T4 (pmol/L)	87.9 ± 2.4	61.1 ± 5.7	55.0 ± 6.9	< 0.001
TSH (mIU/L)	4.5 ± 0.4	2.9 ± 3.2	2.3 ± 0.3	< 0.001

Table 4: *Changes in thyroid hormones following surgery.*





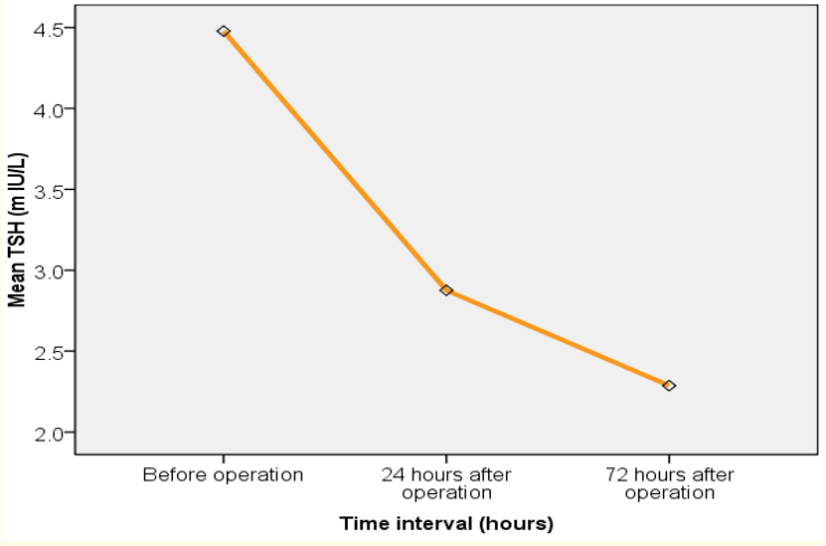


Figure 1: *Changes in serum T3 level from baseline to end-point of the study.*

Discussion

The present study demonstrated that all the study children experienced a significant decline in serum T3, T4 and TSH probably due to NTI syndrome that developed following surgery. The decline was sharp in the first 24 hours in case of serum T4 and TSH and then the decline was slow up to 72 hours. But in case of serum T3, although the decline was steeper in first 24 hours like T4 and TSH, in the next 48 hours it slowly began to rise. In a similar study Babazadeh and colleagues [10] showed that reductions in thyroid hormones following cardiac surgery continued until the 48th postoperative hour, thereupon the thyroid hormones remained in the same level for another day. The reduction in the thyroid hormones might be due to the suppression of TSH release after CPB, which, in turn, might be caused by the changes in the pituitary-thyroid gland axis. In Holland's [11] study, the total levels of T3 and free T3 had a significant decrease in the first 24 hours after the bypass. In addition, the RT3 levels had a four-fold increase of the normal level between 8 - 24 hours after the operation. In another similar study (n = 14), Murzi., *et al*. [12] observed a considerable reduction in the serum levels of T3, T4, free T3, and TSH as well as in the free T3 to free T4 ratio. Allen., *et al.* [13] reported that in 12 children undergoing CPB, there was a significant reduction in the levels of thyroid hormone. In addition, there was a temporary association between the changes made in the metabolisms of these hormones and the severity of the patients' conditions. Overall, each hormone reached its lowest level between 12 to 48 hours after CPB.

In two separate studies, T3, T4, free T4, and TSH were studied in children with congenital heart disease throughout CPB, and up to 48 hours postoperatively. The results showed that T3 and TSH had a significant decrease, whereas free T4 had a postoperative rise [14,15]. Holzer., *et al*. [16] reported that in children undergoing CPB, deiodinase activity diminished with a subsequent reduction in the conversion of T4 to T3 due to a decreasing concentration of plasma selenium. Plumpton and Haas [17] found a significant correlation between the diminishing free T3 and TSH and the length of CPB. Also, they observed that infants who were on ventilation, at least for first 48 postoperative hours, had an average free T3 of 0.9 pmol/L lower than those who were not.

Thus, findings of the present study and those of the other investigators indicate that the changes in the thyroid function were triggered by cardiac surgery using CPB. However, like any other scientific study the present study was limited by small sample size which did not allow us to analyze the factors that might confound the outcome of the study subjects. And as such there was no evidence suggesting that changes in the levels of thyroid hormones after operation could be influenced by factors such as age, gender, weight, postoperative left ventricular ejection fraction, CPB and aortic clamping time, use of ionotropic drugs etc. Finally, there was no evidence suggesting that the reduction in the levels of thyroid hormone after operation depends on type of congenital heart disease. Some investigators have shown that as postoperative illness deteriorates, changes in the levels of thyroid hormone become more significant. However, in such cases, whether thyroid hormone supplementation can result in normalization of thyroid hormone levels has not been rigorously tested. The present study also did not have such scope.

Conclusion

In conclusion, it is clear that the normal function of the thyroid gland is vitally important to the proper function of the cardiovascular system. The transient hypothyroidism that results in patients undergoing cardiac surgery can give rise to bradycardia, a decrease in cardiac output and heart contractility, and an increase in the systematic vascular resistance.1 Several studies have reported that whenever a congenital heart disease has complications, the cardiac operation proves far more difficult. Therefore, it is recommended that thyroid hormones be measured before and after operation in patients with congenital heart disease. However, whether the undesirable outcome of such changes could be treated by exogenous thyroid hormones (Levothyroxine) needs to be further investigated with large randomized clinical trail.

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